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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/572,796	03/21/2006	Christian Steinkuhler	ITR0060YP	5306

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EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/572,796	STEINKUHLER ET AL.	
	Examiner	Art Unit	
	Iqbal H. Chowdhury, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7-20,22 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-5, 7-20, 22 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-2, 4-5, 7-20, 22 and 24 are currently pending in this application.

The preliminary amendment filed on 3/21/2006 is acknowledged.

Applicant's election without traverse of Group I claims 1-2, 4-5, 7-18, 20 22 and 24 in the communication filed on 11/3/2006 is acknowledged. Claims 3, 6, 21, 23 and 25 have been cancelled. Claim 19 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-2, 4-5, 7-18, 20, 22 and 24 are at issue and are present for examination.

Priority

Acknowledgement is made of applicants claim for priority of provisional application 60/506,479 filed on 9/26/2003 and 60/537,729 filed on 1/20/2004.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 3/21/2006 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Drawings

The drawing of this application submitted on 3/21/2006 is accepted by the examiner.

Claim Objections

Claim 4 is objected to as depending from cancelled claim. Appropriate correction is

required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-5, 7-18, 20, 22 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 11, 20 and 22 are directed to a synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes any mammalian heparanase protein.

As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

The specification teaches the structure of only few representative species of such synthetic nucleic acid molecules of SEQ ID NO: 19 encoding human heparanase proteins SEQ ID NO: 16. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding any mammalian heparanase. Given this lack of description of representative species encompassed by the genus, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-2, 4-5, 7-18, 20, 22 and 24 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a synthetic nucleic acid molecule of SEQ ID NO: 19 comprising a sequence of nucleotides that encodes a human heparanase protein of SEQ ID NO: 16, does not reasonably provide enablement for a synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes any mammalian heparanase protein from any source. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-2, 4-5, 7-18, 20, 22 and 24 are so broad as to encompass a synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes any mammalian heparanase protein from any source. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number genes encoding any

heparanase enzymes broadly encompassed by the claims. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only few heparanase genes.

Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes any mammalian heparanase protein from any source. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any heparanase enzyme having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 4-5, 7, 17-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated host cells transformed with the recited nucleic acids does not reasonably provide enablement for host cells within a multicellular animal which have been transformed with the recited nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 4 and 17 are so broad as to encompass host cells transformed with specific nucleic acids, including cell in *in vitro* culture as well as cells within any multicellular organism. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of host cell broadly encompassed by the claims.

While methods for transforming cell *in vitro* are well known in the art, methods for successfully transforming cells within complex multicellular organisms are not routine and are highly unpredictable. Furthermore, methods for producing a successfully transformed cell within one multicellular organism are unlikely to be applicable to transformation of other types of multicellular organisms as multicellular organisms vary widely. However, in this case the disclosure is limited to only host cell in vitro.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including the use of host cells within a multicellular organism for the production of polypeptide. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, expression of genes in a particular host cell having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is suggested that applicants limit the claims to "An isolated host cell".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4-5, 7-18, 20, 22 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Heinrikson et al. (US Patent 6,387,643 B1 published on 5/14/, 2002, claimed priority of US Provisional Application 60/075,706, filed on 2/24/1998). Instant claims are drawn to a synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes a mammalian heparanase protein having two cleavage sites of endoproteinase located between amino acid residues 100 and 168 of the heparanase protein, a vector, host cell and a method of expressing mammalian heparanase, purification and cleavage of the heparanase by endoproteinase.

Heinrikson et al. teach a fusion protein comprising human heparanase, which is 99.9% identical to SEQ ID NO: 16, which encodes pro-heparanase protein having two cleavage sites for proteolytic cleaving propeptide to active processed heparanase protein, which is located at amino acid glu96-Ser97 and glu144-lys145 of human heparanase protein. Heinrickson et al. also teach a vector comprising said gene encoding human heparanase protein with leader sequence, host cell including yeast cell such as Pichia and S. cerevisiae as well as insect cell, mammalian cell, and method of producing human heparanase protein, purification. Heinrikson et al. further teach endoproteinase such as thrombin and cleaving purified human heparanase by thrombin. Heinrickson et al. furthermore, teach fragments of human heparanase including 8 kDa and 50 kDa fragments.

Because the synthetic human heparanase of the instant application and that of the reference is one and the same, Examiner takes the position that the leader sequence which linked the 8 kDa and 50 kDa fragments disclosed in the reference inherently is the same linker sequence as claimed in claim 11, 13-15, 22 and 24. Since the Office does not have the facilities for

examining and comparing applicants' synthetic protein having a specific linker sequence with the fusion protein produced by the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product (i.e. with linker sequence) and the product of the prior art (i.e., with leader sequence). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594. Therefore, Heinrikson et al. anticipate claims 1-2, 4-5, 7-18, 20, 22 and 24 of the instant application.

Claims 1-2, 4-5, 7-18, 20, 22 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Levy-Adam et al. (Heterodimer formation is essential for heparanase enzymatic activity, Biochem Biophys Res Commun. 2003 Sep 5; 308(4): 885-91, see IDS). Instant claims are drawn to a synthetic nucleic acid molecule comprising a sequence of nucleotides that encodes a mammalian heparanase protein having two cleavage sites of endoproteinase located between amino acid residues 100 and 168 of the heparanase protein, having two fragments 8 kDa and 50 kDA with a linker sequence or segment, a vector, host cell and a method of expressing mammalian heparanase, purification and cleavage of the heparanase by endoproteinase.

Levy-Adam et al. teach a fusion protein comprising human heparanase, which is 100% identical to SEQ ID NO: 16, which encodes pro-heparanase protein having two cleavage sites for proteolytic cleaving propeptide to active processed heparanase protein, which is located at amino acid glu109-Ser110 and gln157-lys158 of human heparanase protein with a linking peptide between two fragments of 8 kDa and 50 kDa protein. Levy-Adam et al. also teach a vector comprising said gene encoding human heparanase protein, host cell including insect cell, mammalian cell, and method of producing human heparanase protein, and purification. Levy-

Adam et al. further teach endoproteinase such as thrombin and cleaving purified human heparanase by thrombin. Levy-Adam et al. furthermore, teach fragments of human heparanase including 8 kDa and 50 kDa fragments.

Because the synthetic human heparanase of the instant application and that of the reference is one and the same, Examiner takes the position that the linking peptide sequence which linked the 8 kDa and 50 kDa fragments disclosed in the reference inherently is the same linking sequence as claimed in claim 13-15, 22 and 24. Since the Office does not have the facilities for examining and comparing applicants' synthetic protein having a specific linker sequence with the fusion protein produced by the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product (i.e. with linker sequence) and the product of the prior art (i.e., with linker sequence). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594. Therefore, Levy-Adam et al. anticipate claims 1-2, 4-5, 7-18, 20, 22 and 24 of the instant application.

Conclusion

Status of the claims:

Claims 1-2, 4-5, 7-20, 22 and 24 are pending.

Claims 1-2, 4-5, 7-20, 22 and 24 are rejected.

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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